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Oral Activated Charcoal in the Treatment of Intoxications
Role of Single and Repeated Doses

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Contents

Summary 34
1. Factors Affecting the Antidotal Efficacy of Activated Charcoal 35
1.1 Effects of Physicochemical Properties 35
1.2 Effects of Pharmaceutical Formulation 35
1.3 Effects of Chemical Nature and Formulation of Agents Ingested in Intoxications 35
1.4 Effects of Charcoal Dose 35
1.5 Effect of pH 36
1.6 Gastrointestinal Contents 37
1.7 Effects of Stability of the Charcoal-Poison Complex 38
1.8 Time-Effect Relationships 38
1.9 Effects of Purgatives and Whole-Bowel Irrigation 39
2. Mechanisms of Enhanced Drug and Toxin Elimination by Multiple Charcoal Doses 40
3. Effect of Single and Repeated Doses on the Absorption and Elimination of Drugs in Humans 41
3.1 Antipyretic Analgesics 41
3.2 Other Analgesics 42
3.3 Hypnosedatives and Anticonvulsants 44
3.4 Antidepressants 45
3.5 Other Psychopharmaca 45
3.6 Cardiac Glycosides 46
3.7 Antiarrhythmic Drugs 46
3.8 β-Adrenoceptor Antagonists 47
3.9 Oral Antihyperglycaemic Drugs 47
3.10 Bronchodilating Drugs 47
3.11 Antimicrobial Agents 48
3.12 Hormones 49
3.13 Other Drugs 49
3.14 Metals, Alcohols and Other Substances 51
4. Relative Efficacy of Activated Charcoal, Emetics, and Gastric Lavage in Inhibiting Drug Absorption 52
5. Toxicity and Side Effects of Activated Charcoal 52
6. Conclusions 53
6.1 Role of Single Doses in Treatment of Intoxications 53
6.2 Role of Repeated Doses in Treatment of Intoxications 53

Summary

Activated charcoal has an ability to adsorb a wide variety of substances. This property can be applied to prevent the gastrointestinal absorption of various drugs and toxins and to increase their elimination, even after systemic absorption.

Single doses of oral activated charcoal effectively prevent the gastrointestinal absorption of most drugs and toxins present in the stomach at the time of charcoal administration. Known exceptions are alcohols, cyanide, and metals such as iron and lithium. In general, activated charcoal is more effective than gastric emptying. However, if the amount of drug or poison ingested is very large or if its affinity to charcoal is poor, the adsorption capacity of activated charcoal can be saturated. In such cases properly performed gastric emptying is likely to be more effective than charcoal alone.

Repeated dosing with oral activated charcoal enhances the elimination of many toxicologically significant agents, e.g. aspirin, carbamazepine, dapsone, dextropropoxyphene, cardiac glycosides, meprobamate, phenobarbitone, phenytoin and theophylline. It also accelerates the elimination of many industrial and environmental intoxicants.

In acute intoxications 50 to 100g activated charcoal should be administered to adult patients (to children, about 1 g/kg) as soon as possible. The exceptions are patients poisoned with caustic alkalis or acids which will immediately cause local tissue damages. To avoid delays in charcoal administration, activated charcoal should be a part of first-aid kits both at home and at work. The 'blind' administration of charcoal neither prevents later gastric emptying nor does it cause serious adverse effects provided that pulmonary aspiration in obtunded patients is prevented.

In severe acute poisonings oral activated charcoal should be administered repeatedly, e.g. 20 to 50g at intervals of 4 to 6 hours, until recovery or until plasma drug concentrations have fallen to non-toxic levels. In addition to increasing the elimination of many drugs and toxins even after their systemic absorption, repeated doses of charcoal also reduce the risk of desorbing from the charcoal-toxin complex as the complex passes through the gastrointestinal tract. Charcoal will not increase the elimination of all substances taken. However, as the drug history in acute intoxications is often unreliable, repeated doses of oral activated charcoal in severe intoxications seem to be justified unless the toxicological laboratory has identified the causative agent as not being prone to adsorption by charcoal.

The role of repeated doses of oral activated charcoal in chronic intoxications has not been clearly defined. Charcoal seems able to accelerate the elimination of many industrial and environmental toxicants like dioxins, polychlorinated biphenyls and possibly also some heavy metals, including their radioactive isotopes. Further studies will be needed to define the value of repeated doses of oral activated charcoal in chronic intoxications.

Activated charcoal is an insoluble powder produced by pyrolysis of organic material. It is able to adsorb a wide variety of drugs and toxic agents onto its surface.

The capacity of charcoal to bind chemicals has been recognised for centuries and the first systematic studies of charcoal as an antidote were performed in the early 1800s. During the following hundred years, several studies on activated charcoal were published, but in many countries and in many hospitals its use as an antidote has not been accepted until recently.

One reason for this neglect has been the lack of suitable formulations, a situation which has prevented the use of activated charcoal in adequate amounts. Furthermore, until the 1980s there have been only a few experimental or clinical human studies on the antidotal effect of *high* doses of activated charcoal. The effect of high single and repeated doses of charcoal on the absorption and elimination of various drugs has been studied intensively during the last 10 years. Various aspects of the antidotal use of activated charcoal have been reviewed lately (Cooney 1980; Levy 1982; Neuvonen 1982; Olkkola 1985a; Park et al. 1986; Pond 1986; Spector et al. 1986). As a result, the initial management in particular of intoxicated patients has changed.

Table I. Adsorption of drugs and other substances to activated charcoal *in vitro*

Well adsorbed	Moderately adsorbed	Poorly or clinically inadequately adsorbed
Aflatoxins	Aspirin and other salicylates	Cyanide
Amphetamine	DDT	Ethanol
Antidepressants	Disopyramide	Ethylene glycol
Antiepileptics	Kerosene, benzene and dichlorethane	Iron
Antihistamines	Malathion	Lithium
Atropine	Many 'high-dose' NSAIDs e.g. tolfenamic acid	Methanol
Barbiturates	Mexiletine	Strong acids and alkalis
Benzodiazepines	Paracetamol (acetaminophen)	
β-Blocking agents	PCB-compounds	
Chloroquine and primaquine	Phenol	
Cimetidine	Syrup of ipecacuanha	
Dapsone	Tolbutamide, chlorpropamide, carbutamide,	
Dextropropoxyphene and other opioids	tolazamide	
Digitalis glycosides		
Ergot alkaloids		
Frusemide		
Glibenclamide and glipizide		
Glutethimide		
Indomethacin		
Meprobamate		
Nefopam		
Phenothiazines		
Phenylbutazone		
Phenylpropanolamine		
Piroxicam		
Quinidine and quinine		
Strychnine		
Tetracyclines		
Theophylline		

Abbreviations: NSAID = non-steroidal anti-inflammatory drug; PCB = polychlorinated biphenyl.

1. Factors Affecting the Antidotal Efficacy of Activated Charcoal

1.1 Effects of Physicochemical Properties

Adsorption of chemicals onto charcoal is dependent on several factors. The physicochemical properties of charcoal are of vital importance for its antidotal efficacy. The major determinants of these properties are the pore size and the surface area of charcoal. If all pores are large enough for the drug to enter then the adsorption capacity of charcoal is proportional to its surface area. Modern activated charcoals have a large surface area (1000 to 3500 m^2/g). A usual antidotal dose for adults has an area of more than 10 football fields! Theoretically, recently developed 'superactive' charcoals (area up to 3500 m^2/g) should have a better antidotal efficacy than the conventional ones. There is some evidence for this both *in vitro* and *in vivo* (Cooney 1977a; Cooney & Kane 1980; Chung et al. 1982; Neuvonen et al. 1983d; Park et al. 1984), but the potential advantages in clinical practice of these oil-based charcoals are not clear.

1.2 Effects of Pharmaceutical Formulation

Water suspensions of charcoal are superior to coated charcoal tablets in antidotal use. Uncoated

tablets, as well as plain powdered or specially granulated forms of activated charcoal, can be suspended in water. Adding of thickening and flavouring agents (bentonite and carboxymethylcellulose, saccharin, sorbitol, cherry extract, etc.) to charcoal formulations has resulted in either reduced (De Neve 1976; Mathur et al. 1976a,b; Mayersohn et al. 1977; Yancy et al. 1977), increased (Gwilt & Perrier 1976; Picchioni et al. 1982), or unaffected (Cooney & Roach 1979; Scholtz et al. 1978) adsorption of drugs to activated charcoal.

Some formulations contain significant amounts of ethanol to prevent bacterial growth, sodium bicarbonate to help mixing, or other agents in addition to activated charcoal. These may have some consequences when given in high doses to intoxicated patients.

1.3 Effects of Chemical Nature and Formulation of Agents Ingested in Intoxications

Activated charcoal has the ability to adsorb a wide variety of substances onto its surface, but some substances such as ethanol, iron, lithium and cyanides are not adsorbed in clinically significant amounts (table I). Unfortunately, *in vitro* studies cannot be applied directly in clinical practice. The antidotal efficacy of activated charcoal in humans has to be established by direct human studies.

There seem to be no systematic studies on the ability of activated charcoal to adsorb agents from different pharmaceutical formulations. In healthy volunteers the absorption of a slowly absorbed formulation of phenylpropanolamine 50mg was reduced by 50% only when 25g of charcoal (charcoal-drug ratio 500 : 1) was given immediately after it (Neuvonen & Olkkola 1986). The absorption of 50mg phenylpropanolamine was reduced by 80% when a small dose of 2g of charcoal (charcoal-drug ratio 40 : 1) was ingested immediately after a rapidly absorbing phenylpropanolamine formulation (Tsuchiya & Levy 1972). The apparent discrepancy between these 2 studies is most probably due to the differences in the pharmaceutical formulation of phenylpropanolamine used. The inhibition of the absorption of some other prolonged release formulations (theophylline, valproate) too, has been somewhat lower by a single dose of charcoal than might have been expected (Neuvonen et al. 1983b,c). In some cases the addition of sorbitol or other laxatives to an oral regimen of activated charcoal may decrease serum drug concentrations after the ingestion of slow release formulations (Goldberg et al. 1987).

1.4 Effects of Charcoal Dose

Completeness of adsorption depends greatly on the ratio of charcoal to poison, because according to the mass law there is an equilibrium between free and adsorbed poison. The higher the charcoal-poison ratio, the more complete is the adsorption. At a ratio of 10 : 1, 90 to 100% of most substances are adsorbed in optimum *in vitro* conditions. In acute intoxications the amount and type of poison taken is largely unknown. The less charcoal given, the more easily is its adsorption capacity saturated (figs 1 and 2). Therefore, in the initial management of intoxicated patients large doses (50 to 100g) of charcoal should be used (Neuvonen & Olkkola 1984a; Olkkola 1985b). On the other hand, too large doses of charcoal may cause vomiting and aspiration of charcoal by obtunded patients.

Huge daily doses of 200 to 400g activated charcoal should be given only in well controlled conditions, and only in severe poisoning if necessary. It should be realised that some formulations of activated charcoal may contain considerable amounts of sodium bicarbonate (e.g. 'Medicoal', 1.5g sodium bicarbonate per 5g charcoal), sorbitol (up to 70%) or ethanol, which in high doses may have significant gastrointestinal and systemic side effects.

1.5 Effect of pH

Environmental pH affects the adsorption capacity of activated charcoal. Compounds are best adsorbed to charcoal in their undissociated form,

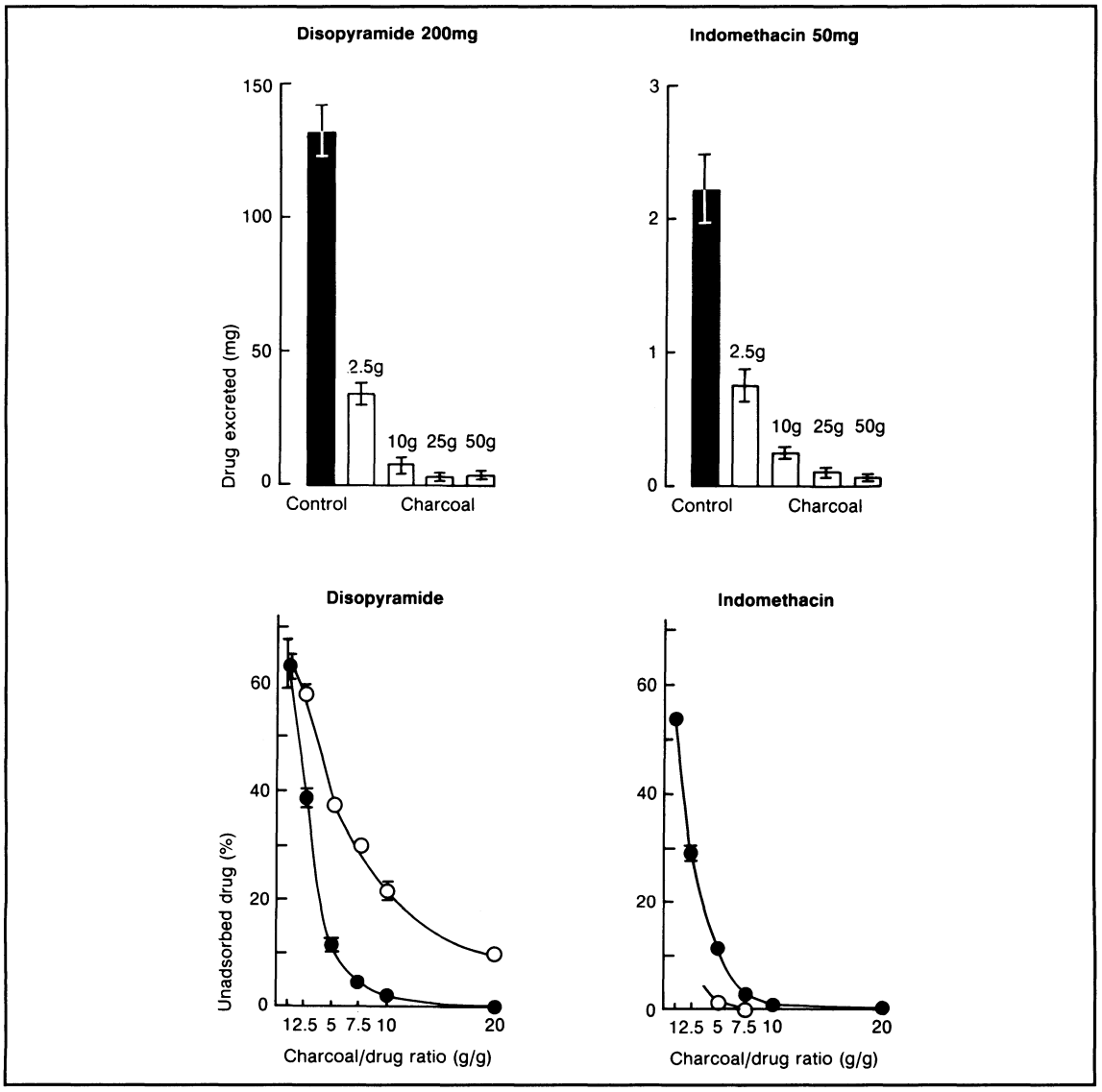

Fig. 1. Top: Effect of different doses of activated charcoal, given after 5 minutes, on the absorption of disopyramide and indomethacin, reflected as their cumulative excretion into urine over 72 hours. Mean ± SEM in 6 volunteers. Bottom: The percentages of unabsorbed disopyramide and indomethacin at pH 1.2 (○) and pH 7.0 (●) and at various charcoal-drug ratios. Mean ± SEM of 3 experiments. From Neuvonen & Olkkola (1984a).

acids at a low pH and bases at a high pH (Andersen 1947; Hauge & Willamann 1927). However, the change in gastric pH has no significant effect on the antidotal efficacy of oral activated charcoal (Olkkola & Neuvonen 1984a).

1.6 Gastrointestinal Contents

Gastrointestinal contents, probably like any other competing solutes, impair the adsorption of drugs to activated charcoal (Andersen 1948). How-

ever, the effect of gastrointestinal contents on the antidotal efficacy of charcoal is complicated. Although the presence of food in the stomach of patients with drug overdosages somewhat impairs the adsorption capacity of charcoal, it gives charcoal more time to effectively adsorb drugs in the gastrointestinal canal (fig. 3), possibly by slowing the gastric emptying rate (Olkkola & Neuvonen 1984b).

Concomitant ethanol ingestion is common in overdosages. Ethanol is an organic solvent and could thus affect the antidotal efficacy of charcoal. Ethanol impairs the adsorption capacity of charcoal *in vitro* but it has only minimal effects in humans (Neuvonen et al. 1984). Accordingly, there should be no hesitation in the administration of activated charcoal to bind other toxic compounds despite the potential ethanol ingestion. Unfortunately, charcoal does not prevent the absorption of ethanol.

1.7 Effects of Stability of the Charcoal-Poison Complex

The binding of drugs and poisons to activated charcoal is a reversible process, meaning that the compound once adsorbed can also desorb (Bainbridge et al. 1977). This has also been demonstrated in humans with certain drugs (Levy & Tsuchiya 1972; Neuvonen & Olkkola 1986; Neuvonen et al. 1978; Olkkola 1985b). The excretion of salicylates into urine from 24 to 72 hours after administration of aspirin has been higher when taken with activated charcoal than without (fig. 4). The apparent half-life of drugs has been prolonged when ingested with a single dose of charcoal (Alvan 1973). This indirectly indicates desorption from charcoal leading to subsequent absorption of the drug. However, if adequately high doses of activated charcoal are used the desorption is seldom significant in clinical situations, but it can somewhat increase the total amount of drug or poison absorbed. The use of repeated doses of charcoal increases its efficacy (Crome et al. 1977; Dawling et al. 1978) and reduces the risk of desorption.

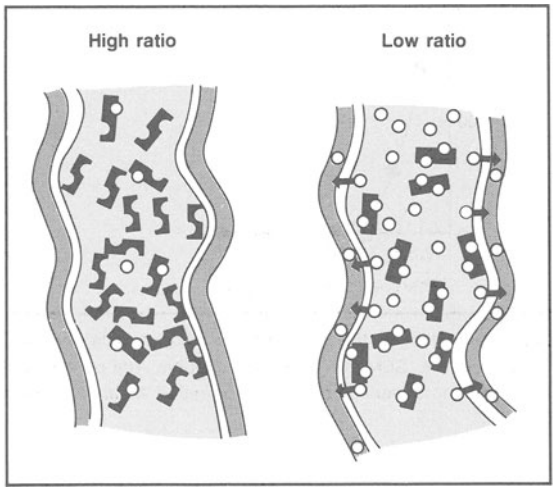

Fig. 2. Schematic representation of the effect of high and low charcoal-drug ratios on systemic drug absorption. At low ratios the amount of free drug (○) and the subsequent absorption from the gastrointestinal tract (▭) into the blood stream (▭) is higher than at high ratios when there is sufficient charcoal (▬) to adsorb the free drug.

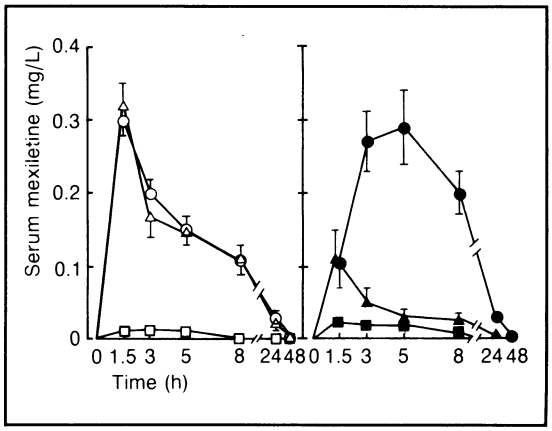

Fig. 3. Effect of activated charcoal and eating on the absorption of 200mg mexiletine, measured by serum mexiletine concentration. Mean ± SEM in 6 volunteers. From Olkkola & Neuvonen (1984b). *Key:* ○ = control; □ = mexiletine + 25g charcoal; △ = mexiletine + charcoal 1 hour later; ● = mexiletine + food; ■ = mexiletine + food + 25g charcoal; ▲ = mexiletine + food + charcoal 1 hour later.

1.8 Time-Effect Relationships

Delay in the administration of charcoal after drug ingestion no doubt impairs the antidotal efficacy of oral activated charcoal. Accordingly, char-

coal should be given as soon as possible and should be a part of first-aid kits both at home and at work.

The rate of absorption of most orally administered agents is directly related to the rate at which these agents pass from the stomach to the intestine (Nimmo 1979). The factors affecting gastric emptying rate and the formulation of the agent ingested thus modify the antidotal efficacy of oral activated charcoal. The absorption of drugs in life-threatening overdosages may be considerably prolonged (Rosenberg et al. 1981). Therefore, there is no exact time at which charcoal should no longer be administered to prevent gastrointestinal absorption in intoxications.

1.9 Effects of Purgatives and Whole-Bowel Irrigation

Theoretically, the quicker a poison passes through the gastrointestinal tract the less will be its desorption, provided that hyperperistalsis and increased fluid secretion do not facilitate desorption. It has been claimed that purgative-enhanced propulsion of charcoal-poison complex would improve the antidotal efficacy of oral activated charcoal. Thus, many authors recommend the use of saline purgatives as an adjunct to charcoal to hasten the elimination of charcoal-poison complex (Boehnert et al. 1985; Cupit & Temple 1984; Daunderer 1983; Krenzelok 1985; Minocha et al. 1985; Oderda 1979; Rumack 1980; Shannon et al. 1986; Teschke 1984).

In animals, purgatives have either improved (Chin et al. 1981; Gaudreault et al. 1985; Laass 1980; Picchioni et al. 1982) or diminished (Galey et al. 1987; Van de Graaff et al. 1982) the antidotal efficacy of charcoal. Most studies in humans have failed to demonstrate any substantial benefit from the combined use of purgatives and charcoal (Easom et al. 1982; Galinsky & Levy 1984; Mayersohn et al. 1977; Neuvonen & Olkkola 1986; Sketris et al. 1982) [fig. 5].

Goldberg et al. (1987) were able to increase the efficacy of repeated doses of oral activated charcoal with sorbitol. They administered charcoal or charcoal combined to sorbitol to healthy volunteers who had taken 1200mg slow release theophylline 6 hours earlier. However, 2 of the 9 subjects developed severe adverse effects (from sorbitol) requiring medical intervention during the charcoal-sorbitol phase. In another recent study (Berg et al. 1987), sorbitol-induced diarrhoea may have accelerated the onset of the effect of charcoal on the elimination of intravenously administered phenobarbitone, although the overall benefit from sorbitol was minimal.

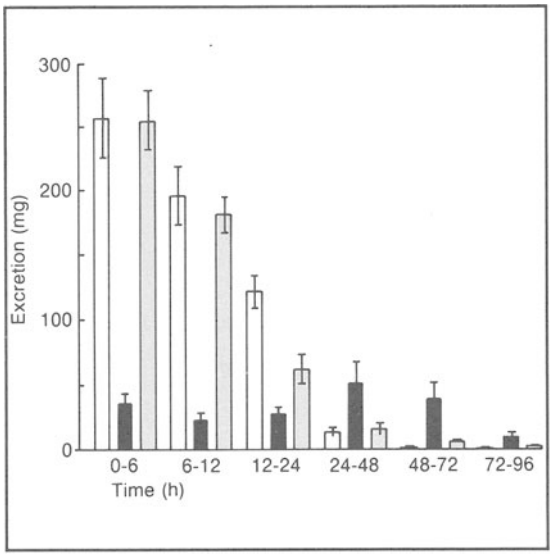

Fig. 4. Effect of activated charcoal (50g), given after 5 minutes (■) or 1 hour (□), on the absorption of aspirin 1000mg, measured by the excretion of salicylate into urine during various periods. Mean ± SEM in 6 volunteers. From Neuvonen et al. (1978). Open bar (□) indicates aspirin excretion without charcoal.

To date, the routine use of purgatives in combination with activated charcoal does not appear to be indicated. Even high doses of activated charcoal given as watery suspensions do not cause constipation in most patients. In fact, charcoal suspensions – without any laxatives – often cause diarrhoea. In some instances the use of laxatives may promote the evacuation of depot formulations or other slowly absorbed drugs from the gastrointestinal tract and thus have a beneficial effect together with activated charcoal. However, the benefits of combining, for example, sorbitol with charcoal must be weighed against the potential risks for the individual patient.

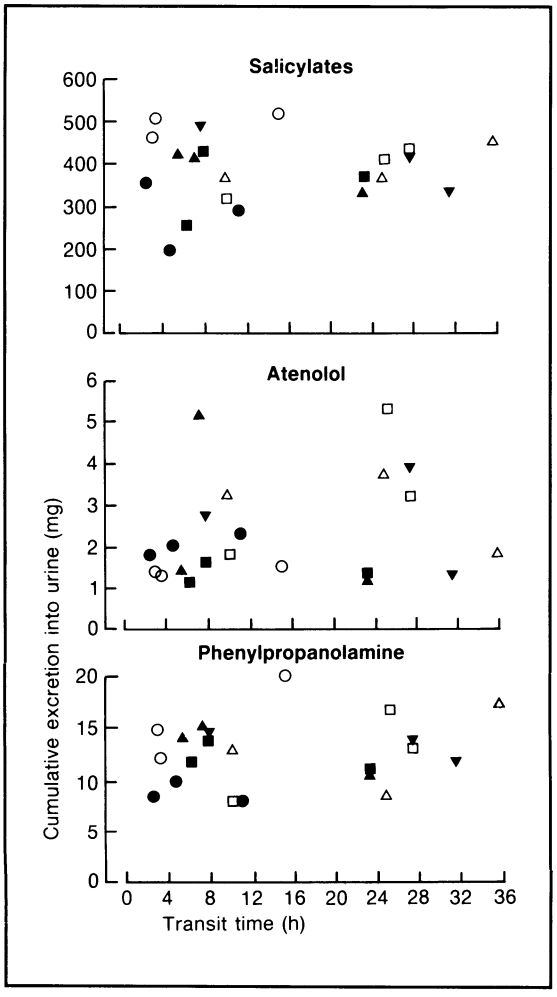

Fig. 5. Correlation between the gastrointestinal transit time (modified by the use of oral magnesium citrate, and rectal metoclopramide and bisacodyl) and the antidotal efficacy of charcoal reflected as the cumulative excretion of salicylates, atenolol and phenylpropanolamine into urine over 36 hours. Different symbols refer to 7 subjects. Activated charcoal (25g) was ingested 5 minutes after aspirin (1000mg), atenolol (100mg) and phenylpropanolamine (50mg). From Neuvonen & Olkkola (1986).

There are some reports of the effect of whole-bowel irrigation on the absorption of drugs and toxic substances from the gastrointestinal tract (Tenenbein et al. 1986). As far as we know, there are no studies on the combined use of whole-bowel irrigation and oral activated charcoal. Theoretically, ingestion of charcoal prior to whole-bowel irrigation, or whole-bowel irrigation with some charcoal added to the irrigation solution, could enhance the efficacy of both charcoal and whole-bowel irrigation.

2. Mechanisms of Enhanced Drug and Toxin Elimination by Multiple Charcoal Doses

Many drugs and toxic agents are excreted into the gastrointestinal tract as parent substances, as active metabolites, or as conjugates, which may liberate active compounds in the gastrointestinal tract. The excretion may occur in gastric juice, bile, pancreatic secretions or other gastrointestinal fluids (McKinnon et al. 1986). Also, the diffusion through the mucosal ('dialysis') membrane from capillaries into the gut is possible. Irrespective of the exact mechanism of the excretion of individual substances, very many of these compounds are then reabsorbed into the blood. Activated charcoal effectively and practically irreversibly adsorbs many of those compounds in the gastrointestinal canal and prevents their reabsorption. The interruption of the enterohepatic and enteroenteric circulation by multiple oral doses of activated charcoal then accelerates the rate of drug elimination (fig. 6).

In some cases the binding of drugs and toxins to a single dose of activated charcoal is far from complete, although the charcoal has been given at an appropriate time. This may be due, for example, to inadequate administration of charcoal, to low affinity of the ingested poisons to charcoal, to the reversibility of adsorption of that particular substance, or to the saturation of the adsorbing capacity of charcoal by the drug or other gastrointestinal tract contents. Furthermore, the release rates of drugs from various pharmaceutical formulations and in various intoxications may vary considerably. This makes the adsorption to a single charcoal dose sometimes less complete than when multiple charcoal doses were given.

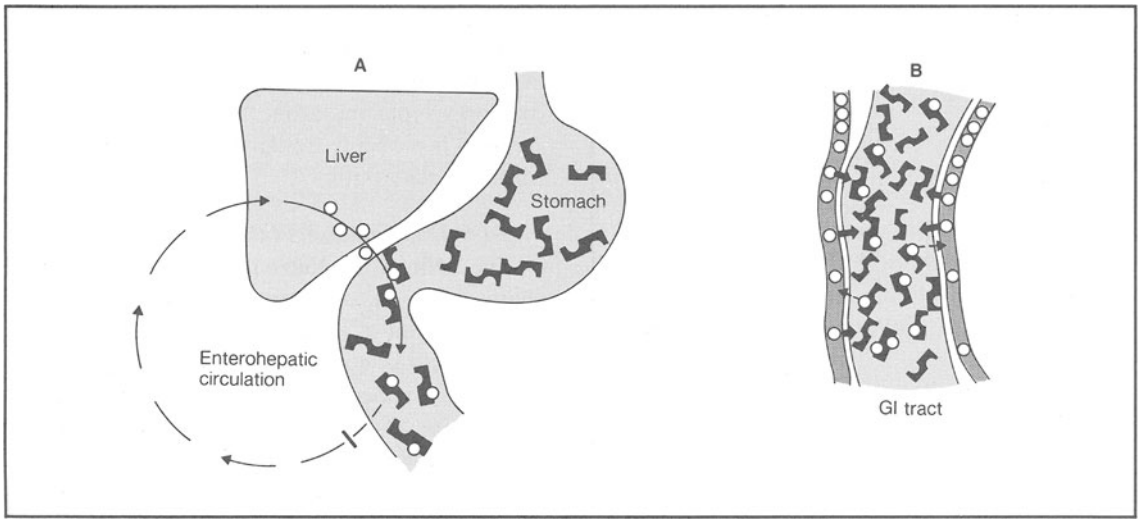

Fig. 6. Orally administered repeat-dose activated charcoal ( ) prevents: (A) the enterohepatic circulation of drugs (○), and (B) favours their diffusion from blood ( ) into gastrointestinal lumen by preventing back-diffusion ('gastrointestinal dialysis').

3. Effect of Single and Repeated Doses on the Absorption and Elimination of Drugs in Humans

3.1 Antipyretic Analgesics

3.1.1 Aspirin

In vitro, aspirin is adsorbed only moderately to activated charcoal. In humans, the absorption of therapeutic aspirin doses (1 to 5g) is reduced by 50 to 85% with 20 to 50g activated charcoal (Levy & Tsuchiya 1972; Neuvonen et al. 1978) [fig. 7].The peak serum concentrations are reduced more effectively, but because of the desorption of aspirin from the aspirin-charcoal complex (fig. 4) the reduction in total absorption is smaller.

Repeated doses of charcoal enhance the elimination of salicylates. This has been shown both in experimental animals (Wogan et al. 1986) and in intoxicated patients (Boldy & Vale 1986; Hillman & Prescott 1985; Prescott et al. 1986). Some charcoal preparations contain considerable amounts of sodium bicarbonate which may contribute to the shortened elimination half-life of salicylates by increasing urinary pH and excretion of salicylates. In any case, repeated doses of charcoal are indicated in aspirin poisoning, as they also reduce the risk of desorption.

3.1.2 Paracetamol

The adsorption of paracetamol to activated charcoal has been studied both *in vitro* and *in vivo* (Dordoni et al. 1973; Galinsky & Levy 1984; Levy & Houston 1976; Neuvonen et al. 1983c). The efficacy of activated charcoal alone has been only moderate in experimental studies (fig. 7) and in paracetamol poisonings saturation of the adsorption capacity of charcoal is likely to occur. In severe paracetamol poisoning specific antidotes, acetylcysteine or methionine, must be used in order to prevent hepatic necrosis. *In vitro* these antidotes are adsorbed to charcoal to some extent (Klein-Schwarz & Oderda 1980). However, this adsorption does not seem to be clinically significant and does not invalidate the concomitant oral administration of charcoal and acetylcysteine (North 1981a; Rybolt et al. 1986).

The elimination half-life of paracetamol is prolonged in severe poisoning. At least theoretically, charcoal may bind paracetamol and its toxic metabolites and thus reduce their hepatic toxicity.

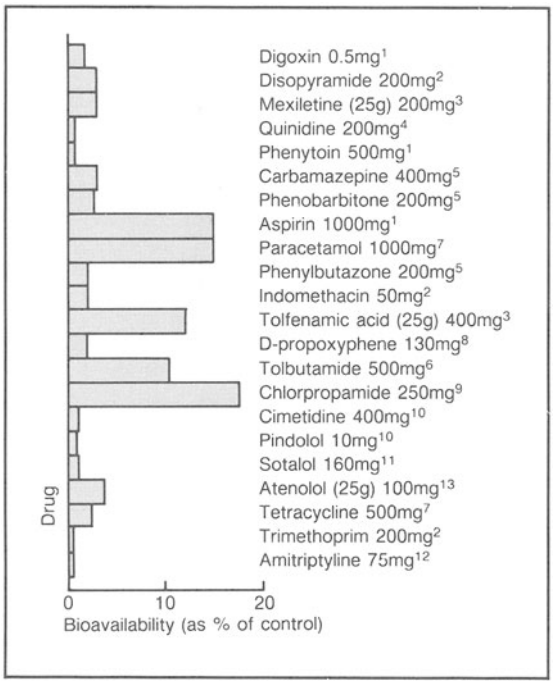

Fig. 7. Inhibition of drug absorption by activated charcoal (Carbomix). Charcoal 50g (except where indicated) or water (control) was ingested 5 minutes after the drug. Mean values in 5 to 7 volunteers. *Reference key:* 1 Neuvonen et al. 1978; 2 Neuvonen & Olkkola 1984a; 3 Olkkola & Neuvonen 1984b; 4 Neuvonen et al. 1984; 5 Neuvonen & Elonen 1980; 6 Neuvonen et al. 1983b; 7 Neuvonen et al. 1983c; 8 Kärkkäinen & Neuvonen 1985; 9 Neuvonen & Kärkkäinen 1983; 10 Neuvonen & Olkkola 1984b; 11 Kärkkäinen & Neuvonen 1984; 12 Kärkkäinen & Neuvonen 1986; 13 Neuvonen & Olkkola 1986.

3.1.3 Indomethacin

Activated charcoal adsorbs indomethacin effectively both *in vitro* and in humans (figs 1 and 7). Saturation of the adsorption capacity of charcoal in indomethacin poisoning is unlikely (Neuvonen & Olkkola 1984a). Large amounts of conjugated indomethacin are excreted into the bile and reabsorbed. It is therefore to be expected that repeated doses of charcoal would enhance its elimination, but this has not been studied.

3.1.4 Phenylbutazone and Other Pyrazolone Derivatives

Activated charcoal inhibits very effectively the absorption of phenylbutazone (fig. 7). The effect of charcoal on the elimination of this drug is only moderate (fig. 8) despite its long elimination half-life (Neuvonen & Elonen 1980). The effect of charcoal on oxyphenbutazone and azapropazone absorption is probably similar to its effect on phenylbutazone absorption.

3.1.5 Tolfenamic Acid (Fenamates)

The affinity of tolfenamic acid to activated charcoal is good, and charcoal moderately prevents the absorption of tolfenamic acid (fig. 7) and mefenamic acid in humans (El-Bahie et al. 1985; Olkkola & Neuvonen 1984a,b). In experimental animals charcoal has also reduced the toxicity of mefenamic acid (Glazko 1967).

The elimination half-life of fenamates is rather short, but some of the metabolites appear to undergo significant enterohepatic circulation and slow elimination. Repeated doses of activated charcoal may enhance the elimination of the fenamate metabolites.

3.1.6 Piroxicam

The absorption of 20mg piroxicam was reduced by 98% by 50g activated charcoal. Repeated oral doses of charcoal shortened the elimination half-life of piroxicam from the control value of 48 hours to 22 hours (Laufen et al. 1984).

3.1.7 Other Antipyretic Analgesics

Activated charcoal is likely to adsorb sulindac, ibuprofen, naproxen and most other antipyretic analgesics, and inhibit their absorption from the gastrointestinal tract. It is to be expected that the enterohepatic circulation of sulindac (Dujovne et al. 1983), and possibly of some other antipyretic analgesics or their metabolites, can be interrupted by activated charcoal. Accordingly, repeated doses of charcoal could enhance the elimination of these drugs.

3.2 Other Analgesics

3.2.1 Dextropropoxyphene

The adsorption of dextropropoxyphene to charcoal is good *in vitro* (Corby & Decker 1968). Activated charcoal 4g, given over 10 to 50 minutes

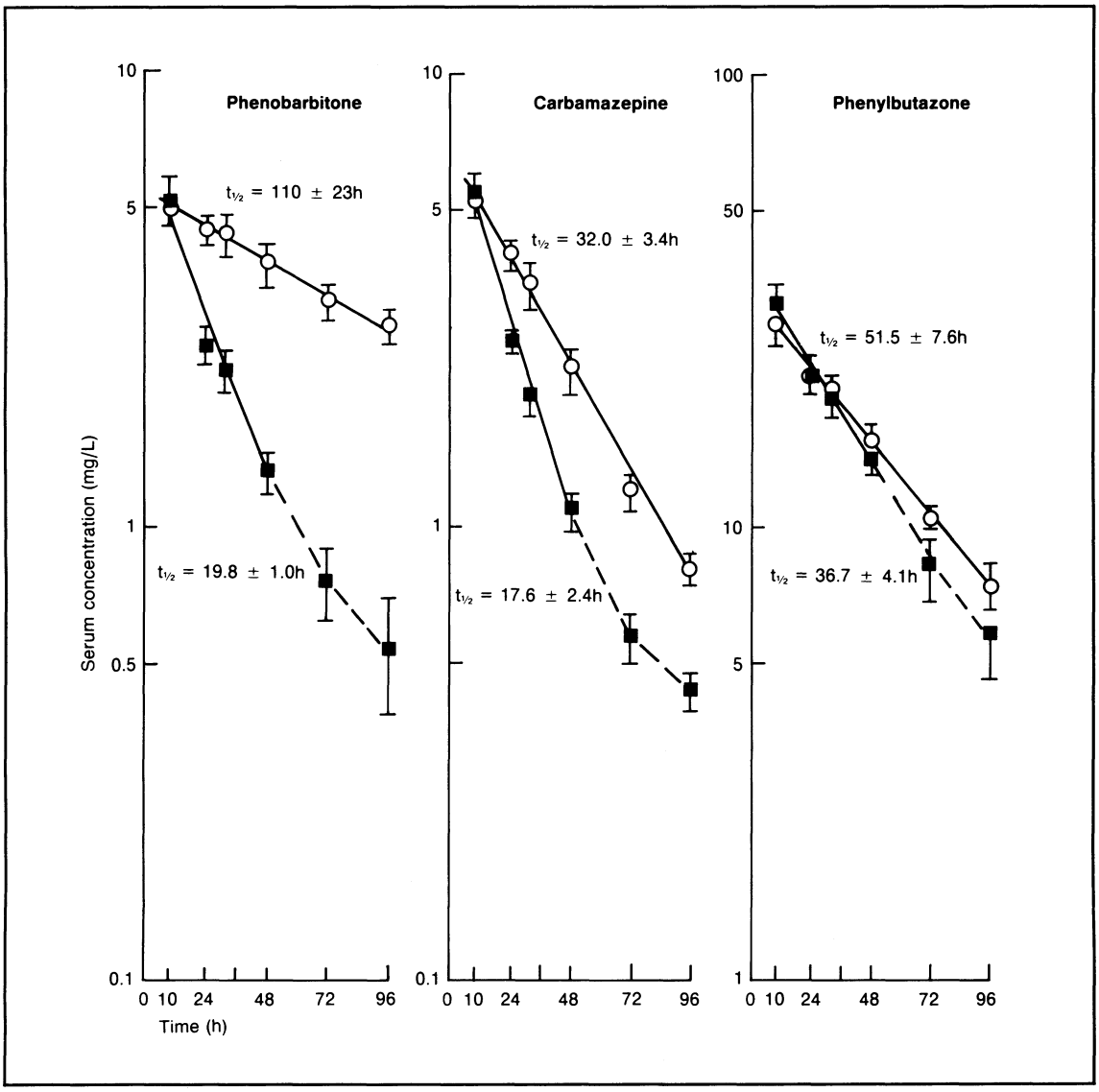

Fig. 8. Effect of activated charcoal (■) given in multiple doses (50g at 10 hours, then 17g at 12, 24, 36 and 48 hours after administration of drug), compared with control (○) on $t_{1/2}$ of phenobarbitone, carbamazepine and phenylbutazone. Mean ± SEM in 5 volunteers. From Neuvonen & Elonen (1980).

after the intake of dextropropoxyphene, reduced its gastrointestinal absorption by 50% (Chernish et al. 1972). 50g charcoal, given immediately after 130mg dextropropoxyphene, reduced its absorption by 97% (Kärkkäinen & Neuvonen 1985) [fig. 7]. It is obvious that 50g activated charcoal can adsorb more than 90% of the dextropropoxyphene present in the stomach of intoxicated patients at the time of the administration of charcoal. Furthermore, repeated doses of oral charcoal will enhance the elimination of both dextropropoxyphene and norpropoxyphene (Kärkkäinen & Neuvonen 1985).

3.2.2 Opiates and Other Opioid Analgesics

There is no reason to believe that activated charcoal would not adsorb morphine, codeine, pentazocine, oxycodone, tilidine (Cordonnier et al. 1986), buprenorphine, methadone and other related substances and inhibit their absorption from the gastrointestinal canal. Because at least methadone and buprenorphine undergo enterohepatic circulation and have a long elimination half-life, charcoal is likely to enhance their elimination, too.

3.2.3 Nefopam

Nefopam has caused several fatal intoxications. It has a good affinity to activated charcoal both *in vitro* and in animals. In mice it has reduced acute toxicity by a factor of 5 (Neuvonen et al. 1983d). The effect of charcoal on the elimination of nefopam is unknown.

3.3 Hypnosedatives and Anticonvulsants

3.3.1 Barbiturates

Activated charcoal binds most barbiturates very effectively. For instance, 50g activated charcoal adsorbed 97% of phenobarbitone (200mg) present in the stomach (Neuvonen & Elonen 1980) [fig. 7].

Normally, phenobarbitone has an elimination half-life of about 100 hours, which repeated doses of oral activated charcoal have shortened to about 20 hours (Neuvonen & Elonen 1980) [fig. 8]. The effect of charcoal has also been shown in intoxicated patients and following intravenous administration of phenobarbitone (Berg et al. 1982, 1987; Goldberg et al. 1985a; Linden et al. 1983; Pond et al. 1984; Vale et al. 1986). Repeated doses of oral activated charcoal should also hasten recovery from phenobarbitone poisoning (Boldy et al. 1986; Goldberg & Berlinger 1982; Prescott et al. 1986; Vale et al. 1986), although that effect was not seen in a controlled study, despite a clear effect on phenobarbitone clearance (Pond et al. 1984). The effect of charcoal on the elimination of other barbiturates has not been studied systematically. In some intoxicated patients elimination has been unaffected by administration of charcoal (Neuvonen 1982).

Orally administered activated charcoal has resulted in a great shortening (80 to 90%), both in half-life and sleep time, in mice following intravenous injection of phenobarbitone (and also of methyprylone, glutethimide, ethchlorvynol and methaqualone), but no significant effect on sleep time following amylobarbitone (amobarbital) or pentobarbitone was noted (Adler et al. 1986).

3.3.2 Meprobamate

Activated charcoal effectively adsorbs meprobamate and inhibits its absorption. Given in multiple doses, charcoal enhances the elimination of meprobamate in overdosages (Hassan 1986; Linden & Rumack 1984).

3.3.3. Benzodiazepines

Charcoal inhibits the absorption of benzodiazepines. Small repeated doses of charcoal did not seem to affect the elimination of diazepam (Korttila et al. 1976). However, 40g oral activated charcoal given 4-hourly seemed to shorten the elimination half-life of diazepam greatly in an intoxicated patient (Traeger & Haug 1986).

3.3.4 Glutethimide

In vitro, glutethimide is efficiently adsorbed to activated charcoal (Decker et al. 1968). Charcoal inhibits the gastrointestinal absorption of glutethimide and probably also increases its elimination (Adler et al. 1986; Fiser et al. 1971; Hayden & Comstock 1975).

3.3.5 Phenytoin

Charcoal effectively inhibits the gastrointestinal absorption of phenytoin. Activated charcoal 50g reduced the gastrointestinal absorption of 500mg phenytoin by 98 to 99% when given after 5 minutes (fig. 7), and by 80% when given 1 hour later (Neuvonen et al. 1978). Because of the slow absorption of phenytoin, charcoal is a useful antidote even several hours after ingestion.

Phenytoin metabolism saturates even at therapeutic doses, and in intoxications elimination is very slow. Repeated doses of charcoal may enhance its elimination (Prescott et al. 1986), al-

though this effect was not clear in another study (Pond et al. 1984).

3.3.6 Carbamazepine

Charcoal inhibits the absorption of carbamazepine effectively in humans. Over 95% of the carbamazepine dose (400mg) present in the stomach was adsorbed to 50g charcoal (Neuvonen & Elonen 1980) [fig. 7]. Repeated charcoal doses have increased the elimination rate of carbamazepine by about 50% in healthy volunteers (Neuvonen & Elonen 1980) [fig. 8] and in intoxicated patients (Boldy et al. 1987; Heath & Van Loo 1986; Vale et al. 1986).

3.3.7 Valproate

The absorption of valproate is inhibited moderately by oral activated charcoal, but not as effectively as that of carbamazepine, phenobarbitone and phenytoin (Neuvonen et al. 1983b). Repeated doses of charcoal also seem to increase its elimination (Prescott et al. 1986).

3.4 Antidepressants

3.4.1 Nortriptyline

Single dose charcoal effectively inhibits the gastrointestinal absorption of nortriptyline but seems to prolong its elimination half-life (Alvan 1973). This suggests desorption of nortriptyline from the charcoal-drug complex, which can be prevented by the administration of repeated doses of activated charcoal (Crome et al. 1977; Dawling et al. 1978). Repeated doses of charcoal may also increase the elimination of nortriptyline to some extent (Kärkkäinen & Neuvonen 1986).

3.4.2 Amitriptyline

Charcoal binds amitriptyline efficiently both *in vitro* and in humans. In healthy volunteers 99% of amitriptyline (75mg) present in the stomach was adsorbed to 50g activated charcoal (Kärkkäinen & Neuvonen 1986) [fig. 7].

Repeated doses of charcoal shortened the elimination half-life of amitriptyline by 20% in healthy volunteers. Elimination of its active metabolite, nortriptyline, was shortened by 40% (Kärkkäinen & Neuvonen 1986). It has been claimed that repeated doses of oral activated charcoal would reduce the elimination half-life of amitriptyline from 40 hours to 4 to 10 hours in intoxicated patients (Swartz & Sherman 1984), but the kinetic data reported do not justify that conclusion. The effect of charcoal on the elimination of amitriptyline is obviously not so dramatic (Prescott et al. 1986).

3.4.3 Imipramine

Charcoal effectively prevents the gastrointestinal absorption of imipramine but did not enhance its elimination (Goldberg et al. 1985b). This may be partly due to the elimination half-life (9 to 10 hours) of imipramine, which is relatively short in comparison with the elimination half-lives of amitriptyline and nortriptyline.

3.4.4 Doxepin

A single dose of 15g activated charcoal administered 30 minutes after doxepin 50mg inhibited 50% of its absorption but caused an apparent prolongation of the elimination half-life. This was due to the desorption of doxepin from charcoal. Repeated doses of charcoal did not reduce the elimination half-life of doxepin, but the clearance of desmethyldoxepin was increased by 57% (Scheinin et al. 1985).

3.4.5 Other Antidepressants

It is to be expected that activated charcoal also inhibits the absorption of other tricyclic and tetracyclic antidepressants. Thus, the immediate administration of charcoal in overdosages with these drugs is certainly indicated and in severe poisoning repeated dosing should be carried out.

3.5 Other Psychopharmaca

3.5.1 Phenothiazines

In vitro, activated charcoal adsorbs the phenothiazines tested well. As little as 100mg activated charcoal mixed with 50mg promazine before ingestion reduced absorption by 60% (Sorby 1965). There is no reason to expect that charcoal would not in-

hibit the absorption of other phenothiazines even better when used in adequate doses. Several phenothiazines have a relatively long elimination half-life and at least some enterohepatic circulation. Accordingly, repeated doses of oral activated charcoal may be useful in acute intoxications.

3.6 Cardiac Glycosides

3.6.1 Digoxin

Charcoal adsorbs digoxin effectively both *in vitro* and in humans. About 98% of therapeutic digoxin doses (0.5mg) was adsorbed to 50g activated charcoal (Neuvonen et al. 1978) [fig. 7]. Activated charcoal may be the most effective treatment in inhibiting the gastrointestinal absorption of digoxin, since the total amount of digoxin ingested is small (less than 100mg) even in severe digoxin poisonings. Thus, the risk of saturation of the adsorption capacity of charcoal is small.

Digoxin undergoes significant enterohepatic cycling in the body, and this can be interrupted by repeated doses of oral activated charcoal. The elimination half-life of digoxin has been shortened by about 50% (fig. 9) by repeat-dose charcoal (Boldy et al. 1985; Lalonde et al. 1985).

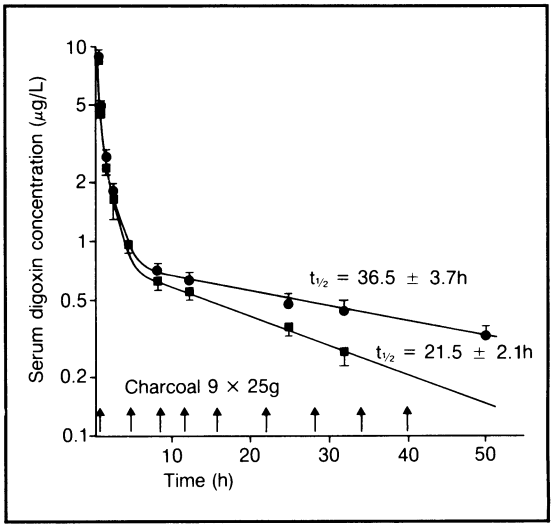

Fig. 9. Serum digoxin concentration during control (●) and charcoal (■) phases. Mean ± SEM in 10 subjects. From Lalonde et al. (1985).

3.6.2 Other Cardiac Glycosides

Activated charcoal effectively adsorbs digitoxin. The relative efficacy of charcoal in digitoxin poisoning is about at the same level as in digoxin poisoning. Digitoxin has a more significant enterohepatic circulation than digoxin, and repeated doses of charcoal have shortened its elimination half-life by 90% (Pond et al. 1981).

The effect of charcoal on the absorption of other cardiac glycosides is probably at the same level as with digoxin and digitoxin. Repeated doses of charcoal may also enhance to some extent the elimination of other cardiac glycosides (Belz & Bader 1974).

3.7 Antiarrhythmic Drugs

3.7.1 Quinidine

Activated charcoal inhibits the gastrointestinal absorption of quinidine very effectively. Charcoal 50g given 5 minutes after quinidine (200mg) reduced its absorption by 99% (Neuvonen et al. 1984) [fig. 7]. The adsorption capacity of charcoal is unlikely to be saturated even in severe quinidine poisoning. Charcoal most likely inhibits the absorption of quinidine more effectively than gastric lavage or ipecac-induced vomiting. Its effect on quinidine elimination is not known, but the elimination of quinidine's optical isomer, quinine, is accelerated by charcoal (Prescott et al. 1986).

3.7.2 Disopyramide

In humans 50g of charcoal prevented the absorption of over 90% of therapeutic doses (200mg) of disopyramide (Neuvonen & Olkkola 1984a). The efficacy of charcoal is also likely to be at least moderate in intoxications, but it should be given in as high doses as feasible to minimise the potential risk of saturation of its adsorption capacity (figs 1 and 7). The effect of charcoal on disopyramide elimination has not been studied.

3.7.3 Mexiletine

Oral activated charcoal inhibits the absorption of mexiletine well in humans. Activated charcoal 25g given 5 minutes after 200mg mexiletine inhib-

ited absorption by over 95% (Olkkola & Neuvonen 1984b) [figs 3 and 7]. Data concerning the effect of charcoal on elimination of mexiletine are lacking.

3.7.4 Other Antiarrhythmic Drugs

Activated charcoal is likely to adsorb most antiarrhythmic drugs and prevent the gastrointestinal absorption of, for example, verapamil, nifedipine, diltiazem, propafenone and amiodarone. The absorption of flecainide 200mg was almost completely prevented when activated charcoal was ingested immediately (Nitsch et al. 1987).

Amiodarone has an exceptionally long elimination half-life and a significant enterohepatic circulation. Thus, repeated doses of oral activated charcoal should be effective in overdosages.

3.8 β-Adrenoceptor Antagonists

In humans, 50g activated charcoal reduced the absorption of atenolol, pindolol and sotalol, given in therapeutic doses, by over 90% (Kärkkäinen & Neuvonen 1984; Neuvonen & Olkkola 1984b, 1986) [fig. 7]. Syrup of ipecac allowed 30-fold greater absorption of pindolol compared with charcoal (Neuvonen & Olkkola 1984b) [fig. 10]. Because of the varying potencies of the β-blocking agents, the amounts ingested in acute overdosages usually range from 100mg (e.g. pindolol) to 10g (e.g. atenolol and sotalol). Based on adsorption studies *in vitro,* it is obvious that the risk of saturation of the adsorption capacity of charcoal is small if the intoxication is caused by a β-blocking agent used therapeutically in small amounts.

Repeated doses of charcoal have been shown to increase elimination of sotalol (Kärkkäinen & Neuvonen 1985) and nadolol (Du Souich et al. 1982).

3.9 Oral Antihyperglycaemic Drugs

Based solely on limited *in vitro* experiments at low pH, where tolbutamide is only sparingly soluble (Decker et al. 1968), activated charcoal was recently erroneously claimed to be ineffective in poisonings caused by tolbutamide (Boyd 1982; Derlet & Albertson 1986). Charcoal effectively adsorbs *in vitro* carbutamide, chlorpropamide, glibenclamide (glyburide), glipizide, tolazamide and tolbutamide (Kannisto & Neuvonen 1984). The

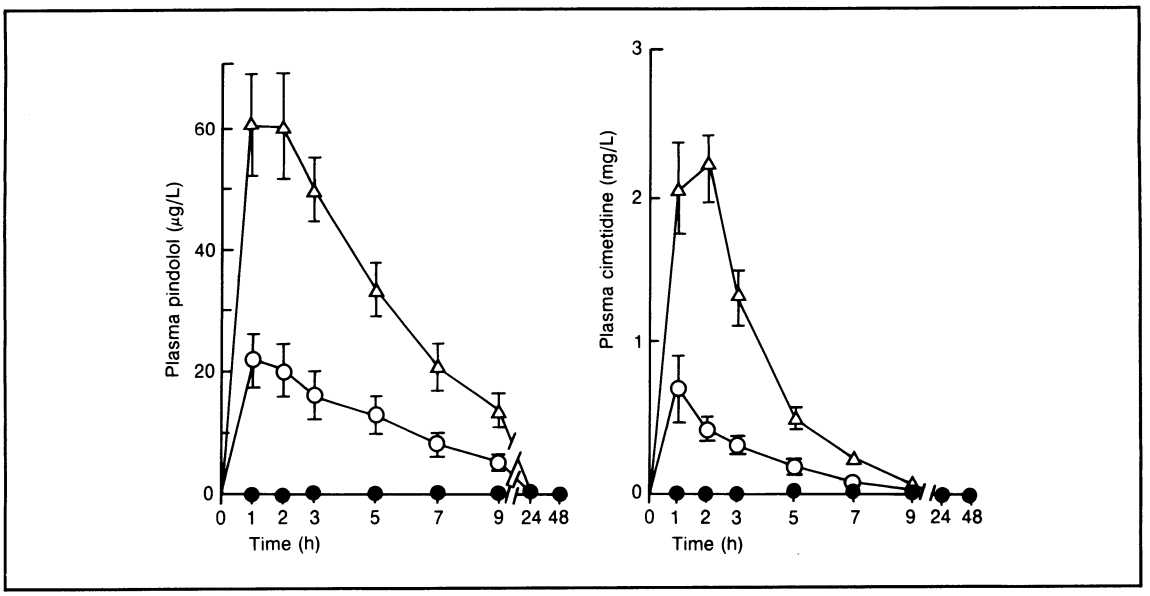

Fig. 10. Effect of activated charcoal (50g) [●] and syrup of ipecac (20ml) [○], given after 5 minutes, compared with control (△), on the absorption of pindolol (10mg) and cimetidine (400mg) as measured by plasma concentration. Mean ± SEM in 7 subjects. From Neuvonen & Olkkola (1984b).

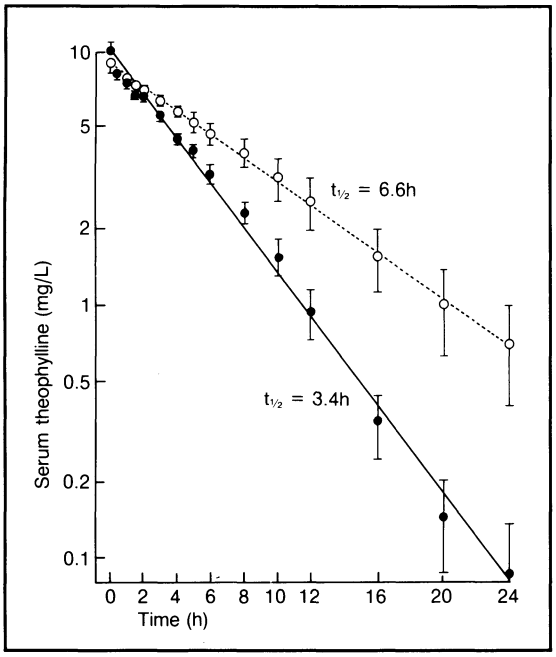

Fig. 11. Serum theophylline concentrations after intravenous infusion of aminophylline (6 mg/kg) with (●) and without (○) activated charcoal (40g at 0 hours and 20g at 2, 4, 6, 9 and 12 hours). Mean ± SEM in 5 subjects. From Berlinger et al. (1983).

adsorption of other sulphonylureas is most likely similar; the affinity of the second generation sulphonylureas to charcoal is especially good. Due to their high potency, therapeutic doses are small, only some milligrams. This results in high charcoal-drug ratios, even in potentially severe overdosages. Accordingly, charcoal is expected to be very effective in intoxications caused by second generation sulphonylureas.

The immediate administration of 50g charcoal inhibited 80 to 90% of the absorption of therapeutic chlorpropamide and tolbutamide doses in healthy volunteers (Neuvonen & Kärkkäinen 1983; Neuvonen et al. 1983b) [fig. 7]. Due to high therapeutic doses of tolbutamide and chlorpropamide, the adsorption capacity of charcoal is likely to be saturated in severe intoxications caused by them (but not by glibenclamide or glipizide).

Repeated doses of charcoal did not enhance the elimination of chlorpropamide (Neuvonen & Kärkkäinen 1983). The effect of charcoal on the elimination of other sulphonylureas has not been studied.

The effect of activated charcoal on the absorption and elimination of biguanides, like buformin, metformin and phenformin, is unknown. On the other hand, repeated doses of charcoal seem to accelerate the elimination of M79175, a new inhibitor of aldose reductase (Arimori et al. 1987).

3.10 Bronchodilating Drugs

Activated charcoal reduces the gastrointestinal absorption of theophylline (Sintek et al. 1979), which is often used as a slowly absorbed preparation. In these cases the efficacy of single charcoal doses is not sufficient to prevent toxicity (Lim et al. 1986; Neuvonen et al. 1983c) and hence repeated doses of charcoal should be used in severe theophylline poisoning to prevent prolonged absorption.

Oral activated charcoal increases the elimination of both orally and intravenously administered theophylline (Gal et al. 1984; Goldberg et al. 1987; Park et al. 1983, 1984; Radomski et al. 1984; Rygnestad et al. 1986 [fig. 11]. However, as theophylline elimination is relatively fast (elimination half-life, 6 to 9 hours), increased elimination may not be as important as it is in poisonings with drugs which have long elimination half-lives. It may be more important to prevent the prolonged gastrointestinal absorption by repeated charcoal doses (fig. 12).

The effect of charcoal on the absorption and elimination of salbutamol (albuterol), terbutaline, and other sympathomimetic drugs is unknown. There is no reason to believe that charcoal would not be effective in preventing absorption of sympathomimetics from the gastrointestinal tract, particularly as their therapeutic doses are small.

3.11 Antimicrobial Agents

Antimicrobial agents are seldom a problem in clinical toxicology. Therefore, interest in the effect of charcoal on the absorption and elimination of these agents has been limited. Oral activated char-

coal inhibits the gastrointestinal absorption of, for example, tetracycline, doxycycline and trimethoprim (Neuvonen & Olkkola 1984a; Neuvonen et al. 1983c; Venho et al. 1978). It also inhibits the absorption of para-aminosalicylic acid, but at low charcoal-drug ratios its adsorption capacity is saturated (Olkkola 1985b). In healthy volunteers, the absorption of isoniazid was poorly inhibited if charcoal was delayed 60 minutes (Scolding et al. 1986). In animals, at a charcoal-drug ratio of 8 : 1, charcoal has effectively reduced the absorption and toxicity of isoniazid and chloroquine (Chin et al. 1970, 1973; Picchioni et al. 1966). Due to the long half-life of chloroquine, multiple dosing of oral charcoal seems to be worth trying in patients with acute or chronic intoxications.

Dapsone is an antimicrobial agent which can cause severe poisoning (Elonen et al. 1979; Reigart et al. 1982). Activated charcoal reduces the gastrointestinal absorption of dapsone and increases the elimination of both dapsone and the metabolite, monoacetyldapsone (Neuvonen et al. 1980). The efficacy of repeat-dose oral charcoal in dapsone intoxications is comparable to that of haemodialysis (Neuvonen et al. 1983a) [fig. 13].

Clioquinol (iodochlorhydroxyquin) seems to undergo enterohepatic circulation in considerable amounts, at least in experimental animals (Kotaki et al. 1984). Because of its potential role in subacute myelo-optic neuropathy, repeated doses of oral activated charcoal should be used in clioquinol overdosages to increase elimination.

3.12 Hormones

Hormones do not have much toxicological significance. Charcoal adsorbs steroid hormones and interferes with the enterohepatic circulation of, for example, oestriol (Heimer & Englund 1986). The concurrent administration of oral contraceptives

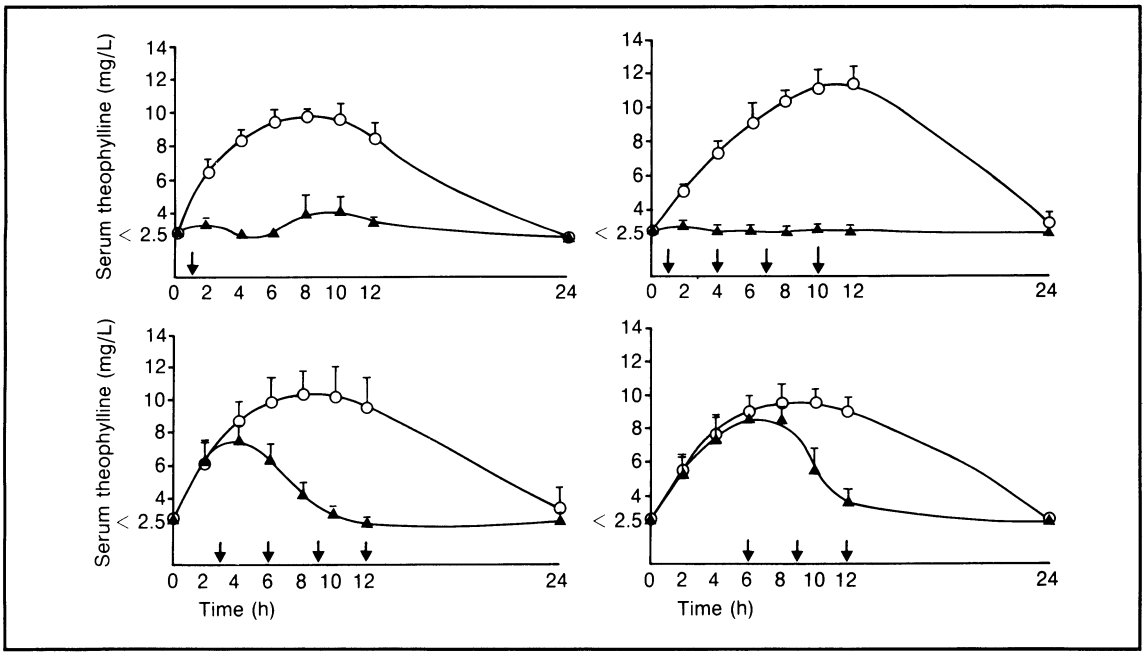

Fig. 12. Serum theophylline concentrations in children (mean age 12 years) after single doses of slow release theophylline (10 mg/kg), with (▲) or without (○) activated charcoal. During the charcoal phase of the crossover study theophylline ingestion was followed by single or repeated doses (1 g/kg) of activated charcoal as indicated by arrows. Mean ± SEM in 5 children in each group. From Lim et al. (1986).

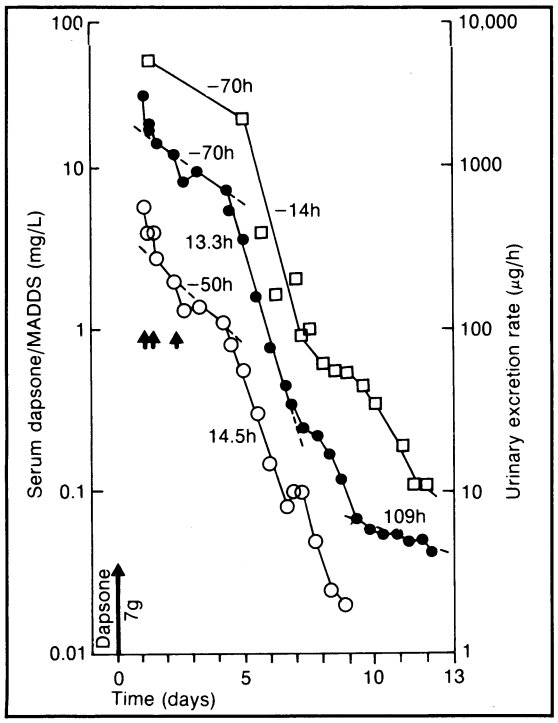

Fig. 13. Effect of orally administered charcoal on serum concentrations of dapsone (●) and monoacetyldapsone (MADDS) [○] and on urinary excretion rate of dapsone (□) in a patient intoxicated with dapsone (70 × 100mg). The first control half-lives on days 1 to 4 are based on the data between 3 haemodialyses (↑ ↑ ↑). The second half-lives are based on the data during charcoal administration (20g 4 times/day) on days 4 to 7. From Neuvonen et al. (1983a).

and charcoal can result in the loss of contraceptive efficacy.

3.13 Other Drugs

3.13.1 Phenylpropanolamine

Phenylpropanolamine has a good affinity to activated charcoal *in vitro* (Tsuchiya & Levy 1972). In humans the absorption of phenylpropanolamine is inhibited well, or at least moderately. Efficacy seems to be dependent on the pharmaceutical formulation of phenylpropanolamine. When a single dose of 25g charcoal was ingested 5 minutes after 50mg phenylpropanolamine as a slowly absorbed formulation, absorption was inhibited by only 50% (Neuvonen & Olkkola 1986). The efficacy of charcoal has been considerably better when a rapidly absorbed formulation is employed (Tsuchiya & Levy 1972). Most probably, charcoal should be given in multiple doses in poisonings caused by slow release formulations of phenylpropanolamine.

3.13.2 Histamine Antagonists

Many classical histamine antagonists (H_1-receptor blockers) have caused severe intoxications. The antihistamines are probably well adsorbed to activated charcoal. Activated charcoal (50g) given within 5 minutes of 200mg diphenylhydramine reduced its absorption by 95% in healthy volunteers (Guay et al. 1984). Astemizole and its active metabolites have an exceptionally long half-life of several days and their elimination could possibly be accelerated by repeat-dose charcoal. The toxicity of H_2-receptor blocking agents is relatively low and, in any case, activated charcoal effectively prevents the gastrointestinal absorption of cimetidine, for example (Neuvonen & Olkkola 1984b) [figs 7 and 10].

3.13.3 Diuretics

The epoxide metabolites of frusemide (furosemide) may cause hepatic necrosis in high overdoses. A small dose of charcoal (8g) completely prevented (99.5%) the absorption of a therapeutic dose (40mg) of frusemide (Neuvonen et al. 1987). Thus, the usual antidotal dose of charcoal binds even high toxic doses of frusemide well. The absorption of thiazide diuretics can probably also be prevented by activated charcoal. Some thiazide diuretics and chlorthalidone undergo significant enterohepatic circulation, which could be affected by repeat-dose charcoal.

3.13.4 Propantheline

Activated charcoal 5g ingested simultaneously with 45mg propantheline significantly reduced the pharmacological effects, suggesting an inhibition of propantheline absorption (Chaput de Saintonge & Herxheimer 1971).

3.13.5 Methotrexate

Activated charcoal adsorbs methotrexate well, both *in vitro* and in humans. Repeated doses of oral charcoal also increase its elimination (Gadgil et al. 1982), which could have some clinical significance with high dose methotrexate treatment in patients with renal failure.

3.13.6 Cyclosporine

Oral activated charcoal is able to adsorb cyclosporine and to increase its elimination (Honcharic & Anthone 1985).

3.13.7 Syrup of Ipecac

Charcoal adsorbs the active ingredients of syrup of ipecac (Cooney 1978). However, when a 5-minute delay occurred between the administration of syrup of ipecac (60ml, i.e. twice the usual dose) and activated charcoal (50g), ipecac-induced emesis occurred in 80% of subjects (Krenzelok et al. 1986). In a clinical study, activated charcoal (50g), given 10 minutes after syrup of ipecac (60ml), did not prevent the emetic effect in any of the 10 intoxicated patients (Freedman et al. 1987).

3.13.8 Acetylcysteine and Methionine

Although *in vitro* acetylcysteine and methionine are adsorbed slightly to activated charcoal (Klein-Schwarz & Oderda 1980) the absorption of acetylcysteine is not prevented by oral charcoal in man (North et al. 1981a; Rybolt et al. 1986).

3.14 Metals, Alcohols and Other Substances

3.14.1 Metals

The efficacy of charcoal in human metal poisoning has not been studied. Some metallic salts, mercuric chloride for example, seem to be fairly well adsorbed *in vitro* (Andersen 1945). Orally administered multiple-dose charcoal may increase the elimination of some metals from the body. However, most metals, including lithium and iron, are not efficiently adsorbed to activated charcoal.

3.14.2 Alcohols

Activated charcoal adsorbs *in vitro* up to 300 to 400mg ethanol per gram of charcoal (Andersen 1947; Smith et al. 1967). In dogs, charcoal significantly reduced (or possibly only postponed) the absorption of ethanol (North et al. 1981b). However, in humans charcoal does not significantly affect the absorption of ethanol (Hulten et al. 1986; Minocha et al. 1986; Neuvonen et al. 1984). Although some reviews (Cupit & Temple 1984) still claim that ethanol is well adsorbed to charcoal, activated charcoal is not an effective antidote against ethanol intoxication.

The efficacy of charcoal in methanol poisoning seems to be comparable to its low efficacy in ethanol poisoning (Picchioni 1970). However, there are few experimental data on the effect of charcoal on methanol toxicity.

In animals, activated charcoal seems to reduce the mortality in ethylene glycol poisoning (Szabuniewicz et al. 1975), even though *in vitro*, charcoal adsorbs ethylene glycol relatively inefficiently (Cooney 1977b). This apparent discrepancy may be caused by the toxic metabolites of ethylene glycol, which in acute poisoning may be of major importance (Jacobsen & McMartin 1986).

3.14.3 Other Substances

Activated charcoal binds well to paraquat *in vitro*. In animals charcoal is at least as effective as Fuller's earth in reducing the toxicity of paraquat (Gaudreault et al. 1985; Okonek et al. 1982), but its antidotal efficacy in human paraquat poisoning has not been studied. The absorption and toxicity of T-2 mycotoxin is reduced by activated charcoal even if some time (e.g. 3 hours in the rat) has elapsed since exposure (Galey et al. 1987).

High doses of oral activated charcoal also reduce gastrointestinal absorption of kerosene, benzene and dichlorethane in rats (Chin et al. 1969; Laass 1980). The effect of repeated doses of charcoal on the elimination of paraquat, kerosene, benzene, dichlorethane and other organic solvents is unknown.

Activated charcoal adsorbs many other substances well (table I), including nicotine, strychnine

and aflatoxins (Decker & Corby 1980). However, cyanide is not adsorbed significantly to charcoal. Even pretreatment with charcoal does not reduce the toxicity of potassium cyanide in mice (Neuvonen, unpublished results).

4. Relative Efficacy of Activated Charcoal, Emetics, and Gastric Lavage in Inhibiting Drug Absorption

Induced emesis seems to be more efficient than gastric lavage in emptying the stomach (Abdallah & Tye 1967; Arnold et al. 1959; Boxer et al. 1969; Corby et al. 1967). The validity of these older studies has been questioned because of the later technical development in orogastric tubes. It has been claimed that currently used large orogastric tubes are able to remove larger volumes of gastric contents than the previously used tubes (Burke 1972; Wheeler-Usher et al. 1986). However, the question remains whether gastric emptying should be performed at all.

Kulig et al. (1985) have demonstrated that syrup of ipecacuanha does not alter the clinical course of poisoned patients who are alert on presentation to hospital. Recent experimental studies have shown that oral activated charcoal is superior to emetics in reducing the absorption of that fraction of the drug which is still present in the stomach when charcoal or emetic is administered (Curtis et al. 1984; Neuvonen & Olkkola 1984b; Neuvonen et al. 1983c) [figs 10 and 14]. In these studies therapeutic doses (from 10 to 2000mg) of various drugs have been used. Despite the apparent handicap of experimental studies when compared with clinical intoxications, the data are relevant to very many intoxications: most drugs will cause fatal intoxications in doses of a few grams, or even in much smaller doses. However, it is obvious that gastric emptying is likely to be more effective than activated charcoal alone in those poisonings where the amount of the drug ingested is large (e.g. aspirin and paracetamol poisonings) leading to saturation of the adsorption capacity of charcoal, or where the affinity of the particular agent to activated charcoal is poor (e.g. iron, table I).

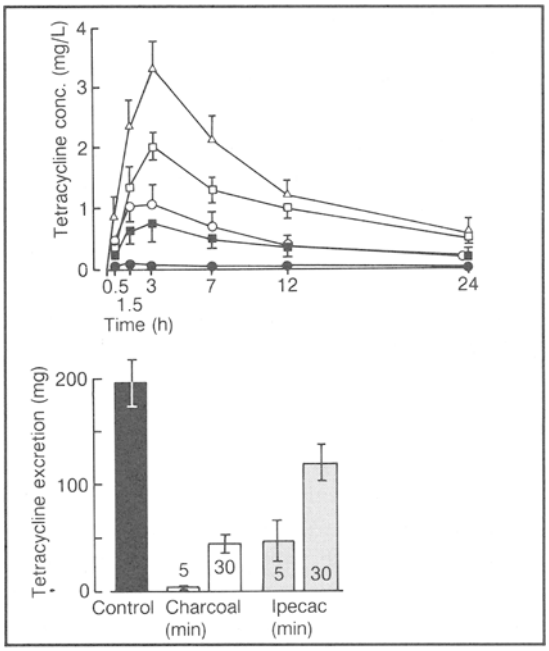

Fig. 14. Effect of activated charcoal (50g) given after 5 (●) or 30 (○) minutes, and syrup of ipecac (20ml) given after 5 (■) or 30 minutes (□), compared with tetracycline alone (△) on the absorption of tetracycline (500mg), reflected as serum concentration and 48 hours' cumulative excretion of tetracycline. Mean ± SEM in 3 volunteers. Tetracycline excretion was significantly less after charcoal than in the control group ($p < 0.01$), and was significantly less with charcoal after 5 minutes than ipecac after 5 minutes ($p < 0.05$) or charcoal after 30 minutes than ipecac after 30 minutes ($p < 0.01$). From Neuvonen et al. (1983c).

The immediate administration of activated charcoal before other time-consuming procedures should be considered in most intoxications. The efficacy of charcoal is expected to be good in poisonings where adsorption capacity will not be saturated, and its administration does not prevent gastric emptying being performed later. Charcoal in the stomach can adsorb drugs which otherwise could be absorbed to systemic circulation during transport to hospital and during the gastric emptying procedures.

5. Toxicity and Side Effects of Activated Charcoal

Activated charcoal has not of itself been associated with specific toxicity (Nau et al. 1958a,b, 1962). In uraemic patients continuous treatment

with oral charcoal 20 to 50 g/day over periods of 4 to 20 months has not resulted in any significant side effects (Yatzidis 1972), although rapid ingestion of large doses of charcoal may cause vomiting. Constipation or sometimes diarrhoea have occurred in some subjects receiving activated charcoal as a watery suspension.

Major complications associated with the use of activated charcoal have been due to the aspiration of charcoal and gastric contents (Harsch 1986; Pollack et al. 1981). There has been at least 1 case of charcoal-containing empyema (Justiniani et al. 1985) and 1 case of intestinal obstruction caused by huge amounts (300g) of charcoal (Anderson & Ware 1987). Possible constipation caused by activated charcoal can be treated with sorbitol, paraffin oil or lactulose. It should be noted that activated charcoal adsorbs many laxatives (e.g. sennosides) and prevents their action.

Some commercially available charcoal preparations contain large amounts of sorbitol or sodium bicarbonate. Repeated administration of these preparations in high doses may cause severe adverse effects (hypotension, electrolyte disturbances), themselves requiring medical intervention (Goldberg et al. 1987). Thus, the use of various extra agents in combination with activated charcoal must be weighed against the potential risks.

6. Conclusions

6.1 Role of Single Doses in Treatment of Intoxications

Single doses of oral activated charcoal effectively (or in some cases very effectively) prevent the gastrointestinal absorption of that fraction of most drugs and poisons which is present in the stomach when charcoal is given. Known exceptions are alcohols, cyanide, and metals such as iron and lithium.

In general, activated charcoal is superior to emetics in reducing absorption. If the amount of drug or poison ingested is large (e.g. aspirin and paracetamol poisonings) or if its affinity to charcoal is poor (e.g. iron poisoning), the adsorption capacity of activated charcoal can be saturated. In those instances, properly performed gastric emptying is likely to be more effective than charcoal alone.

In acute intoxications the drug history is often unreliable and thus, to be on the safe side, overtreatment is necessary. Although there is no exact time after which charcoal should not be administered to prevent gastrointestinal absorption, activated charcoal should be administered orally to acutely poisoned patients (adults 50 to 100g, children 1 g/kg) as soon as possible. The only exceptions are probably patients poisoned with caustic alkalis and acids. To avoid unnecessary delays in administration, activated charcoal should be a part of first-aid kits both at home and at work. In obtunded patients charcoal can be administered with a gastric tube, but tracheal intubation may be needed prior to administration. The 'blind' administration of charcoal neither prevents later gastric emptying nor does it cause serious adverse effects, as long as pulmonary aspiration in obtunded patients is prevented. Accordingly, there is nothing to prevent the liberal administration of charcoal in the immediate management of a poisoned patient.

6.2 Role of Repeated Doses in Treatment of Intoxications

6.2.1 Acute Intoxications

Repeated dosing with oral activated charcoal enhances the elimination of aspirin, carbamazepine, cyclosporine, dapsone, dextropropoxyphene, digitoxin, digoxin, meprobamate, nadolol, nortriptyline, phenobarbitone, phenytoin, piroxicam, valproate, sotalol and theophylline, to give some examples. It is to be expected that the efficacy of charcoal in accelerating the elimination of many other substances will be shown in the near future. Repeated doses of charcoal also reduce the risk of poison desorbing from the charcoal-poison complex.

Repeated dosing with oral activated charcoal seems to be indicated in severe poisonings until recovery or until plasma concentrations have fallen to non-toxic levels. Often doses of 20 to 50g activated charcoal as a watery suspension are given every 4 to 6 hours for 1 to 2 days. Constipation is

seldom a problem but laxatives, such as sorbitol or lactulose, can be given with charcoal.

6.2.2 Chronic Intoxications

Repeated doses of oral activated charcoal may prove very useful in accelerating the elimination of many industrial and environmental toxicants, like dioxins, polychlorinated biphenyls, and some heavy metals and their radioactive isotopes, thus reducing the long term adverse effects of these toxicants. Moderate doses of activated charcoal, e.g. 10 to 20g every 6 to 8 hours, can be used for several months without significant side effects, although possible interference with gastrointestinal absorption of essential therapeutic drugs should be kept in mind during charcoal use. Further studies are needed to establish the value of repeated doses of oral activated charcoal in various types of chronic intoxications.

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